L Number	Hits	Search Text	DB	Time stamp
1	810	((low adj molecular adj weight) lmw) adj heparin	USPAT; US-PGPUB	2002/09/06 13:03
2	2210	cerebral adj ischemia	USPAT; US-PGPUB	2002/09/06 13:03
3	1827	cerebral adj infarct$6	USPAT; US-PGPUB	2002/09/06 13:04
4	3598	(cerebral adj ischemia) (cerebral adj infarct$6)	USPAT; US-PGPUB	2002/09/06 13:04
5	152562	stroke	USPAT; US-PGPUB	2002/09/06 13:04
6	154109	((cerebral adj ischemia) (cerebral adj infarct$6)) stroke	USPAT; US-PGPUB	2002/09/06 13:04
7	249	(((low adj molecular adj weight) lmw) adj heparin) and (((cerebral adj ischemia) (cerebral adj infarct$6)) stroke)	USPAT; US-PGPUB	2002/09/06 13:52
8	118	enoxaparin	USPAT; US-PGPUB	2002/09/06 13:52
9	21	((((low adj molecular adj weight) lmw) adj heparin) and (((cerebral adj ischemia) (cerebral adj infarct$6)) stroke)) and enoxaparin	USPAT; US-PGPUB	2002/09/06 14:01
10	2478	cerebral adj (ischemia infarct$6)	EPO; JPO; DERWENT	2002/09/06 14:02
11	4909	heparin	EPO; JPO; DERWENT	2002/09/06 14:02
12	5	enoxaparin	EPO; JPO; DERWENT	2002/09/06 14:02
13	4910	heparin enoxaparin	EPO; JPO; DERWENT	2002/09/06 14:02
14	1948	ischemi$4 and stroke	EPO; JPO; DERWENT	2002/09/06 14:03
15	6453	(cerebral adj (ischemia infarct$6)) adn (ischemi$4 and stroke)	EPO; JPO; DERWENT	2002/09/06 14:03
16	420	(cerebral adj (ischemia infarct$6)) and (ischemi$4 and stroke)	EPO; JPO; DERWENT	2002/09/06 14:03
17	4006	(cerebral adj (ischemia infarct$6)) (ischemi$4 and stroke)	EPO; JPO; DERWENT	2002/09/06 14:04
18	88	((cerebral adj (ischemia infarct$6)) (ischemi$4 and stroke)) and (heparin enoxaparin)	EPO; JPO; DERWENT	2002/09/06 14:04

(FILE 'HOME' ENTERED AT 15:08:40 ON 06 SEP 2002)

FILE 'MEDLINE' ENTERED AT 15:08:46 ON 06 SEP 2002

FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 15:08:57 ON 06 SEP 2002

L1	4361	S	ENOXAPARIN
L2	30409	S	CEREBRAL ISCHEMIA
L3	18	S	L1 AND L2
L4	8	DUP REM	L3 (10 DUPLICATES REMOVED)

L4 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:453216 BIOSIS
DOCUMENT NUMBER: PREV200200453216
TITLE: **Enoxaparin** vs heparin for prevention of deep-vein thrombosis in acute ischaemic stroke: A randomized, double-blind study.
AUTHOR(S): Hillbom, M. (1); Erila, T.; Sotaniemi, K.; Tatlisumak, T.; Sarna, S.; Kaste, M.
CORPORATE SOURCE: (1) Department of Neurology, Oulu University Hospital, FIN-90220, Oulu: matti.hillbom@oulu.fi Finland
SOURCE: Acta Neurologica Scandinavica, (August, 2002) Vol. 106, No. 2, pp. 84-92. http://www.blackwellmunksgaard.com/actaneurologica. print.
ISSN: 0001-6314.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Objectives - To compare the efficacy, safety, and overall risk-benefit profile of **enoxaparin** and unfractionated heparin (UFH) prophylaxis of venous thromboembolic complications in patients with acute ischaemic stroke. Methods - Patients with ischaemic stroke resulting in lower-limb paralysis lasting for at least 24 h and necessitating bedrest, were randomized within 48 h of the onset of stroke, and treated with **enoxaparin** (40 mg subcutaneously once daily) or UFH (5000 IU subcutaneously thrice daily) for 10 +- 2 days. Main outcome measures were deep-vein thrombosis, pulmonary embolism (PE), death from any cause, intracranial haemorrhage including haemorrhagic infarction, or any other major bleeding. Results - Outcome events occurred within 3 months of stroke in 40/106 patients treated with **enoxaparin** (37.7%) and 52/106 patients treated with UFH (49.1%, P = 0.127). Fewer patients treated with **enoxaparin** (14, 13.2%) than with UFH (20, 18.9%) had evidence of haemorrhagic transformation of ischaemic stroke. Conclusions - **Enoxaparin** administered subcutaneously once daily was as safe and effective as subcutaneous UFH given thrice daily in the prevention of thromboembolic events in patients with lower limb paralysis caused by acute ischaemic stroke.

L4 ANSWER 2 OF 8 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002327171 MEDLINE
DOCUMENT NUMBER: 22065155 PubMed ID: 12070524
TITLE: Neuroprotective profile of **enoxaparin**, a low molecular weight heparin, in in vivo models of **cerebral ischemia** or traumatic brain injury in rats: a review.
AUTHOR: Stutzmann Jean-Marie; Mary Veronique; Wahl Florence; Grosjean-Piot Odile; Uzan Andre; Pratt Jeremy
CORPORATE SOURCE: Aventis Pharma, Neurodegenerative Disease Group, 13, Quai Jules Guesde, 94400 Vitry-sur-Seine, France.. jean-marie.stutzmann@aventis.com
SOURCE: CNS Drug Rev, (2002 Spring) 8 (1) 1-30. Ref: 84
Journal code: 9514898. ISSN: 1080-563X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020619
Last Updated on STN: 20020810
Entered Medline: 20020809
AB The development of treatments for acute neurodegenerative diseases (stroke and brain trauma) has focused on (i) reestablishing blood flow to ischemic areas as quickly as possible (i.e. mainly antithrombotics or thrombolytics for stroke therapy) and (ii) on protecting neurons from cytotoxic events (i.e. neuroprotective therapies such as anti-excitotoxic or anti-inflammatory agents for stroke and neurotrauma therapies). This paper reviews the preclinical data for **enoxaparin** in in vivo models of ischemia and brain trauma in rats. Following a photothrombotic lesion in the rat, **enoxaparin** significantly reduced edema at 24 h after lesion when the treatment was started up to 18 h after insult. **Enoxaparin** was also tested after an ischemic insult using the

transient middle cerebral artery occlusion (tMCAO) model in the rat. **Enoxaparin**, 2 x 1.5 mg/kg i.v., significantly reduced the lesion size and improved the neuroscore when the treatment was started up to 5 h after ischemia. **Enoxaparin**, administered at 5 h after insult, reduced cortical lesion size in a dose-dependent manner. In permanent MCAO, **enoxaparin** (5 and 24 h after insult) significantly reduced lesion size and improved neuroscore. A slight and reversible elevation of activated partial thromboplastin time (APTT) suggests that **enoxaparin** is neuroprotective at a non-hemorrhagic dose. Traumatic brain injury (TBI) is often accompanied by secondary ischemia due in part to edema-induced compression of blood vessels. When **enoxaparin**, at 0.5 mg/kg i.v. + 4 x 1 mg/kg s.c., was administered later than 30 h after TBI, it significantly reduced edema in hippocampus and parietal cortex. At one week after TBI the lesion size was significantly reduced and the neurological deficit significantly improved in **enoxaparin** treated animals. Finally, the cognitive impairment was significantly improved by **enoxaparin** at 48 h to 2 weeks after TBI. The anticoagulant properties of unfractionated heparin and specifically **enoxaparin** can explain their anti-ischemic effects in experimental models. Furthermore, unfractionated heparin and specifically **enoxaparin**, have, in addition to anticoagulant, many other pharmacological effects (i.e. reduction of intracellular Ca2+ release; antioxidant effect; anti-inflammatory or neurotrophic effects) that could act in synergy to explain the neuroprotective activity of **enoxaparin** in acute neurodegenerative diseases. Finally, we demonstrated, that in different in vivo models of acute neurodegenerative diseases, **enoxaparin** reduces brain edema and lesion size and improves motor and cognitive functional recovery with a large therapeutic window of opportunity (compatible with a clinical application). Taking into account these experimental data in models of ischemia and brain trauma, the clinical use of **enoxaparin** in acute neurodegenerative diseases warrants serious consideration.

L4 ANSWER 3 OF 8 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001228900 MEDLINE
DOCUMENT NUMBER: 21180468 PubMed ID: 11283402
TITLE: **Enoxaparin** in experimental stroke: neuroprotection and therapeutic window of opportunity.
AUTHOR: Mary V; Wahl F; Uzan A; Stutzmann J M
CORPORATE SOURCE: CNS Research, Aventis Pharma, CRVA, Vitry-sur-seine, France.. veronique.mary@aventis.com
SOURCE: STROKE, (2001 Apr) 32 (4) 993-9.
Journal code: 0235266. ISSN: 1524-4628.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010521
Entered Medline: 20010426

AB BACKGROUND AND PURPOSE: Heparin and heparinoids have long been proposed for stroke treatment. This study investigates the effect of **enoxaparin** (Lovenox, Clexane), a low-molecular-weight heparin, on functional outcome (neuroscore) and lesion size in stroke models with reversible and irreversible **cerebral ischemia** using middle cerebral artery occlusion (MCAO) in the rat. METHODS: Ischemia was induced in rats by transient occlusion for 2 hours or by permanent electrocoagulation of the left MCA. Forty-eight hours after ischemia, neurological deficit was evaluated by scoring sensorimotor functions and ischemic damage was quantified by histological evaluation of lesion volumes. RESULTS: After transient MCAO, **enoxaparin** at 2x1.5 mg/kg IV (2 and 24 hours after insult) significantly reduced lesion size by 30% ($P<0.05$) and improved neuroscore ($P<0.01$). This significant effect on lesion size and neuroscore was still evident when treatment was started 5 hours after insult. Administered under the same protocol with a 5 hours delay post permanent MCAO, **enoxaparin** reduced lesion size by 49% ($P<0.05$) and improved neuroscore ($P<0.01$). CONCLUSIONS: This study indicates that standard nonhemorrhagic doses of **enoxaparin** reduce ischemic damage with a wide therapeutic window. In addition to its anticoagulant properties, other properties of **enoxaparin** could act in synergy to explain its neuroprotective profile in ischemia. Thus

clinical application of **enoxaparin** treatment in stroke warrants serious consideration.

L4 ANSWER 4 OF 8 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000511513 MEDLINE
DOCUMENT NUMBER: 20517820 PubMed ID: 11062276
TITLE: Safety and cost of low-molecular-weight heparin as bridging anticoagulant therapy in subacute **cerebral ischemia**.
AUTHOR: Kalafut M A; Gandhi R; Kidwell C S; Saver J L
CORPORATE SOURCE: Division of Neurology, Scripps Clinic, La Jolla, CA, USA.. mkalafut@scrippsclinic.com
CONTRACT NUMBER: K24 NS 02092-01 (NINDS)
SOURCE: STROKE, (2000 Nov) 31 (11) 2563-8. Journal code: 0235266. ISSN: 1524-4628.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010521
Entered Medline: 20001121

AB BACKGROUND AND PURPOSE: Anticoagulation with intravenous unfractionated heparin (IVUH) while awaiting therapeutic oral anticoagulant levels is a common practice in patients with acute and subacute **cerebral ischemia**. A promising alternative strategy is to use bridging subcutaneous low-molecular-weight heparin (LMWH), which may have a favorable risk-benefit profile compared with IVUH and may permit earlier discharge with completion of transition to warfarin therapy as an outpatient. METHODS: A LMWH, **enoxaparin** 1 mg/kg BID, was used as bridging anticoagulation therapy in 24 consecutive patients admitted to a university stroke center in whom the treatment plan included transition from acute to chronic anticoagulation. The LMWH group was contrasted with the preceding 24 patients transitioned to warfarin with IVUH at the same center. RESULTS: Fewer patients in the LMWH bridging therapy group experienced neurological worsening than in the IVUH bridging therapy group (2/24 versus 8/24; P:=0.033). Fewer total adverse events were noted in the LMWH group than in the IVUH cohort (3 versus 20; P:=0. 002). Fifteen of the 24 LMWH patients (62.5%) were discharged while still receiving LMWH and completed transition to warfarin as outpatients, receiving an average of 3.6 days of outpatient transitional therapy. In these 15 patients, use of LMWH was associated with a net savings of $2197 per patient. CONCLUSIONS: In this pilot cohort with subacute **cerebral ischemia**, bridging LMWH appeared to be safer than bridging IVUH and was associated with reduced hospital stay and reduced total cost of care.

L4 ANSWER 5 OF 8 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000483984 MEDLINE
DOCUMENT NUMBER: 20336809 PubMed ID: 10876084
TITLE: **Enoxaparin**, a low molecular weight heparin decreases infarct size and improves sensorimotor function in a rat model of focal **cerebral ischemia**.
AUTHOR: Quartermain D; Li Y; Jonas S
CORPORATE SOURCE: Department of Neurology, New York University School of Medicine, 550 St. Avenue, New York, USA.. quartd01@popmail.med.nyu.edu
SOURCE: NEUROSCIENCE LETTERS, (2000 Jul 14) 288 (2) 155-8. Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001010

AB Possible neuroprotective effects of the low molecular weight heparin (LMWH) **enoxaparin** sodium (Lovenox) were evaluated in a rat model of focal ischemia. Male Sprague-Dawley rats were subjected to 90 min of

occlusion of the right middle cerebral artery using the intraluminal suture method. **Enoxaparin** at doses of 0, 10 or 15 mg/kg was administered to groups of rats 1, 8, 24 and 32 h after artery occlusion. Motor impairment was evaluated by performance on the traverse beam and accelerating rotarod tests. Animals were sacrificed 48 h after occlusion and brain sections were stained with 2% 2,3,5-triphenyltetrazolium chloride for determination of infarct volume. Forty percent of the rats receiving 15 mg/kg **enoxaparin** died as a result of intracranial hemorrhage. Untreated rats exhibited large lesions involving the caudate putamen and much of the cortex. In **enoxaparin** - treated rats the damage was mainly confined to the caudate putamen. The sensorimotor behavior of the 10 mg/kg **enoxaparin** group was significantly better than that of untreated animals. Motor performance of the survivors in the 15 mg/kg group was poor due to hypoactivity and weakness resulting from excessive bleeding. These results suggest that LMWH may have a neuroprotective function.

L4 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:42949 BIOSIS
DOCUMENT NUMBER: PREV200000042949
TITLE: **Enoxaparin** is superior to unfractionated heparin in the prevention of thromboembolic events in medical patients at increased thromboembolic risk.
AUTHOR(S): Harenberg, J. (1); Schomaker, U. (1); Flosbach, C. W.
CORPORATE SOURCE: (1) Medizinische Klinik, Universitatsklinikum, Mannheim Germany
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 399a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:42935 BIOSIS
DOCUMENT NUMBER: PREV200000042935
TITLE: Comparison of the efficacy and safety of the low-molecular-weight heparin **enoxaparin** with unfractionated heparin in the prevention of deep vein thrombosis in patients with acute ischemic stroke.
AUTHOR(S): Hillbom, M. (1); Erila, T.; Sotaniemi, K. (1); Flosbach, C. W.; Tatlisumak, T.; Sarna, S.; Kaste, M.
CORPORATE SOURCE: (1) University Central Hospital, Oulu Finland
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 183a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 8 OF 8 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999189226 MEDLINE
DOCUMENT NUMBER: 99189226 PubMed ID: 10087432
TITLE: **Enoxaparin** reduces cerebral edemaafter photothrombotic injury in the rat.
AUTHOR: Pratt J; Boudeau P; Uzan A; Imperato A; Stutzmann J
CORPORATE SOURCE: CNS Research, Rhone-Poulenc-Rorer, Vitry-sur-Seine, France.. jeremy.pratt@rp-rorer.fr
SOURCE: HAEMOSTASIS, (1998 Mar-Apr) 28 (2) 78-85.
Journal code: 0371574. ISSN: 0301-0147.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 20000303
Entered Medline: 19990615

AB This study investigates the effect of **enoxaparin** (Lovenox, Klexane), a low-molecular-weight heparin, on edema following a photothrombotic lesion using rose bengal dye in the rat. An area of **cerebral ischemia** was provoked in the right hemisphere of rats. Edema developed over 24 h after the lesion, as seen comparing water content of a core sample from the right hemisphere to that of a similar sample from the left hemisphere of each rat. **Enoxaparin** at 0. 5 mg/kg i.v. plus 2 mg/kg s.c. reduced edema 24 h after lesion induction by 32% ($p < 0.01$) when the treatment was started 2 h after photothrombotic insult, with maintenance doses of 2 mg/kg s.c. **enoxaparin** at 6 and 18 h. When the same initial treatment with **enoxaparin** was started 18 h after insult, there was still a significant reduction of 20% ($p < 0.01$) in cerebral edema. Administration of **enoxaparin** 18 h after insult reduced cerebral edema in a dose-dependent manner. There was no evidence of intracranial hemorrhages in any of the animal groups and when the hemoglobin content of the brain samples was assayed by the method of Drabkin, no increase in hemoglobin content was seen compared to sham-operated animals.